

Inventor: Glen A. Evans

Serial No.: 10/611,655

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AMENDMENTS

On page 4, please delete the paragraph beginning on line 17 through line 26, and substitute therefore:

Figure 1 shows the design and sequence of a ThyOx family non-immunoglobulin binding polypeptide. Figure 1A shows an amino acid alignment of Thy-1 (SEQ ID NO: 1) and an antibody variable heavy chain (SEQ ID NO: 2) region together with a deduced Ig-like domain containing scaffold consensus amino acid sequence (SEQ ID NO: 3). Figure 1B shows the amino acid sequence of ThyOx non-immunoglobulin binding polypeptide containing CDR binding domains (SEQ ID NO: 4). Figure 1C shows a diagram of the ThyOx non-immunoglobulin binding polypeptide.

On page 4, please delete the paragraph beginning on line 27 through page 5, line 2, and substitute therefore:

Figure 2 shows a schematic diagram (Figure 2A), amino acid sequence (Figure 2B; SEQ ID NO: 6), and the nucleotide sequence and corresponding amino acid sequence (Figure 2C; SEQ ID NOS: 5 and 6, respectively) of a chimeric ThyOx carrier polypeptide containing erythropoietin.

On page 5, please delete the paragraph beginning on line 3 through line 4, and substitute therefore:

Figure 3 shows a schematic diagram (Figure 3A) and the nucleotide and amino acid sequence of SuperEpo (Figure 3B; SEQ ID NOS: 7 and 8, respectively).

On page 5, please delete the paragraph beginning on line 5 through line 9, and substitute therefore:

Figure 4 shows a schematic diagram (Figure 4A), amino acid sequence (Figure 4B; SEQ ID NO: 10), and the nucleotide sequence and corresponding amino acid sequence (Figure 4C; SEQ ID NOS: 9 and 10, respectively) of a chimeric ThyOx carrier polypeptide containing glucagon-like peptide 1.

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On page 5, please delete the paragraph beginning on line 10 through line 11, and substitute therefore:

Figure 5 shows a schematic diagram (Figure 5A) and the nucleotide sequence for the vector pEgea M3 (Figure 5B; SEQ ID NO: 11).

On page 5, please delete the paragraph beginning on line 12 through line 13, and substitute therefore:

Figure 6 shows a schematic diagram (Figure 6A) and the nucleotide sequence for the vector pEgea Q6 (Figure 6B; SEQ ID NO: 12).

On page 81, please delete the paragraph beginning on line 10 through line 21, and substitute therefore:

A non-immunoglobulin Epo-Thy1 carrier binding polypeptide was designed to consist of the following components: modified human Epo at the amino terminal end of the mature polypeptide consisting of amino acid substitutions increase activity ("superEpo"); a human Epo leader sequence at the amino terminus, followed by a synthetic linker (GGGGS)₃ (SEQ ID NO: 13); followed by mature human soluble Thy-1 (without Thy-1 leader sequence and transmembrane tail), and the inclusion of a 6X His tag at the carboxyl terminal end of the molecule. A schematic diagram of the resultant chimeric Epo-Thy1 carrier binding polypeptide is shown in Figure 2A.

On page 82, please delete the paragraph beginning on line 9 through line 14, and substitute therefore:

For construction of the non-immunoglobulin Epo-Thy1 carrier binding polypeptide the human Epo leader was retained for expression in mammalian cells. A synthetic linker was incorporated following the leader that was based on the anti-fibrin single chain antibody (GGGGS)₃ synthetic linker (SEQ ID NO: 13) in ScFv1.9.

On page 84, please delete the paragraph beginning on line 1 through line 10, and substitute therefore:

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A non-immunoglobulin GLP-Thy1 carrier binding polypeptide was designed to consist of a GLP-1 peptide fused to the amino terminus of a Thy1 scaffold polypeptide used as a carrier as described in Example II. A (G₄S)₃-like linker (SEQ ID NO: 13) separated the two polypeptide sequences as described in Example II. The leader sequence and Thy1 carrier polypeptide sequence was as described in Example II. A schematic diagram of the resultant chimeric GLP-Thy1 carrier binding polypeptide is shown in Figure 4A.

On page 84, please delete the paragraph beginning on line 21 through line 31, and substitute therefore:

For construction of the non-immunoglobulin GLP-Thy1 carrier binding polypeptide, the human GLP-1 peptide amino acid sequence was used as a starting place equivalent to amino acids 98-127 of the mature preproglucagon, amino acids 1-31. The second amino acid residue (A₂) of GLP-1 was replaced by a G₂ from extendin-4, to eliminate the DPP IV peptidase cleavage site (Dipeptidyl aminopeptidase IV). A synthetic linker was incorporated following the GLP sequence that was based on the anti-fibrin single chain antibody (GGGGS)₃ synthetic linker (SEQ ID NO: 13) in ScFv1.9.